WHAT IS CLAIMED IS:

1. A compound of Formula (1.0.0):

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(1.0.0)

— wherein —

-g is 0 or 1;

-j is 0 or 1; provided that when j is 0, n must be 2;

10 -k is 0 or 1

-m is 0, 1, or 2;

-n is 1 or 2;

-W¹ is -O-; or -S(=O)_t-, where t is 0, 1, or 2; or -N(R³)- where R³ has the same meaning as defined below;

15 -W² is -O-; -S(=O)_t-, where t is 0, 1, or 2; -N(R³)- where R³ has the same meaning as defined below, or -CR²⁹R³⁰-;

- where -

- --R²⁹ and R³⁰ are each a member independently selected from the group consisting of -H; -F; -CF₃; -(C₁-C₃) alkyl; -(C₃-C₆) cycloalkyl; phenyl; benzyl; and pyridyl; wherein said alkyl, cycloalkyl, phenyl, benzyl, and pyridyl moieties are each independently substituted with 0 to 3 substituents R¹⁰, where R¹⁰ has the same meaning as defined below;
- -Y is =C(R¹_a)—, where R¹_a has the same meaning as defined below; or -[N \Rightarrow (O)_k]— where k is 0 or 1;

- where -

-- R_a^1 is a member selected from the group consisting of -H; -F; -Cl; -CN; -NO₂; -(C₁-C₄) alkyl; -(C₂-C₄) alkynyl; fluorinated--(C₁-C₃) alkyl; fluorinated-(C₁-C₃) alkoxy; -OR¹⁶; and -C(=O)NR²²_aR²²_b;

- where -

- - -R^A and R^B are each a member independently selected from the group consisting of -H; -F; -CF₃; -(C₁-C₄) alkyl; -(C₃-C₇) cycloalkyl; phenyl; and benzyl; wherein said cycloalkyl, phenyl, and benzyl moieties are each independently substituted with 0 to 3 substituents R¹⁰;

- where -

-- R^{10} is a member selected from the group consisting of phenyl; pyridyl; -F; -Cl; -CF₃; oxo (=0); -OR¹⁶; -NO₂; -CN; -C(=0)OR¹⁶; -O-C(=0)R¹⁶; -C(=0)NR¹⁶R¹⁷; -NR¹⁶C(=0)R¹⁷; -NR¹⁶C(=0)OR¹⁷; -NR¹⁶S(=0)₂R¹⁷; and -S(=0)₂NR¹⁶R¹⁷; where said phenyl or pyridyl is substituted by 0 to 3 R¹¹;

- where -

--- R^{11} is -F; -CI; -CF₃; -CN; -NO₂; -OH; -(C₁-C₃) alkoxy; -(C₁-C₃) alkyI; or -NR¹⁶R¹⁷:

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---- R^{16} and R^{17} are each a member independently selected from the group consisting of -H; $-(C_1-C_4)$ alkyl; $-(C_2-C_4)$ alkenyl; $-(C_3-C_6)$ cycloalkyl; phenyl; benzyl; and pyridyl; wherein said alkyl, alkenyl, cycloalkyl, phenyl, benzyl, or pyridyl is substituted by 0 to 3 substituents selected from the group consisting of -F, -Cl, $-CF_3$, -CN, and $-(C_1-C_3)$ alkyl;

25 — or —

-R^A and R^B are taken together, but only in the case where m is 1, to form a spiro moiety of Formula (1.2.0):

(1.2.0)

— where —

--r and s are independently 0 to 4 provided that the sum of r + s is at least 1 but not greater than 5;

— and —

--X^A is selected from -CH₂-, -CH(R¹¹)-, or C(R¹¹)₂-, where each R¹¹ is selected independently of the other and each has the same meaning as defined above; -NR¹⁵-, where R¹⁵ has the same meaning as defined below; -O-; and -S(=O)_t-, where t is 0, 1, or 2;

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— and —

said spiro moiety of partial Formula (1.2.0) is substituted as to any one or more carbon atoms thereof, other than that defining X^A, by 0 to 3 substituents R¹⁴, where R¹⁴ has the same meaning as defined below; as to a nitrogen atom thereof by 0 or 1 substituent R¹⁵, where R¹⁵ has the same meaning as defined below; and as to a sulfur atom thereof by 0 or 2 oxygen atoms;

- -R^C and R^D have the same meaning as defined above for R^A and R^B except that one of them must be -H, and they are selected independently of each other and of R^A and R^B;
- -R¹ and R² may individually or together appear on any ring or rings comprising a meaning of the moiety Q² as defined below; and R¹ and R² are each a member independently selected from the group consisting of –H; –F; –Cl; –CN; –NO₂; –(C₁-C₄) alkyl; –(C₂-C₄) alkynyl; fluorinated–(C₁ -C₃) alkyl; –OR¹⁶; and -C(=O)NR²²_aR²²_b; where R¹⁶, R²²_a, and R²²_b have the same meanings as defined above;
- 25 -R³ is -H; -(C₁-C₃) alkyl; phenyl; benzyl; or -OR¹⁶, where R¹⁶ has the same meaning as defined above;
 - -R⁴, R⁵ and R⁶ may individually or together appear on any ring or rings comprising a meaning of the moiety Q¹ as defined below; and R⁴, R⁵ and R⁶ are each a member independently selected from the group consisting of

- the following: -

- where -

- --p is 0, 1, or 2; and R^{22}_{a} , R^{16} , and R^{17} have the same meanings as defined above;
 - -(b) -(C₁-C₄) alkyl; and -(C₁-C₄) alkoxy in the case where one or more of R^4 , R^5 , or R^6 has the meaning of -OR¹⁶ under (a) above and R^{16} is defined as -(C₁-C₄) alkyl; wherein said alkyl and alkoxy are each independently substituted with 0 to 3 substituents –F or –Cl; or 0 or 1 substituent (C₁-C₂) alkoxycarbonyl–; (C₁-C₂) alkylcarbonyloxy–;

— and —

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an aryl or heterocyclyl moiety selected from the group consisting of phenyl; benzyl; furanyl; tetrahydrofuranyl; oxetanyl; thienyl; tetrahydrothienyl; pyrrolyl; pyrrolidinyl; oxazolyl; oxazolidinyl; isoxazolyl; isoxazolyl; thiazolyl; thiazolyl; isothiazolyl; isothiazolyl; pyrazolyl; pyrazolyl; pyrazolyl; pyrazolyl; pyridazinyl; thiadiazolyl; imidazolyl; imidazolyl; imidazolyl; pyridinyl; pyridinyl; pyridinyl; pyridinyl; pyridinyl; piperazinyl; triazolyl; triazinyl; tetrazolyl; pyranyl; azetidinyl; morpholinyl, parathiazinyl; indolyl; indolinyl; benzo[b]furanyl; 2,3-dihydrobenzofuranyl; 2-H-chromenyl; chromanyl; benzothienyl; 1-H-indazolyl; benzimidazolyl; benzoxazolyl; benzisoxazolyl; benzthiazolyl; quinolinyl; isoquinolinyl; phthalazinyl; quinazolinyl; quinoxalinyl; and purinyl; wherein said aryl and heterocyclyl moieties are each independently substituted with 0 to 2 substituents R¹⁴

--- where ---

-- R^{14} is a member selected from the group consisting of $-(C_1-C_4)$ alkyl; $-(C_3-C_7)$ cycloalkyl; phenyl; benzyl; pyridyl; and quinolinyl; where said alkyl, cycloalkyl, phenyl, benzyl, pyridyl, or quinolinyl is substituted by 0, 1, or 2 substituents -F, -Cl, $-CH_3$, $-OR^{16}$, $-NO_2$, -CN, or $-NR^{16}R^{17}$; and said R^{14} group further consists of -F; -Cl; $-CF_3$; oxo (=O); $-OR^{16}$; $-NO_2$; -CN; $-C(=O)OR^{16}$; $-O-C(=O)R^{16}$; $-C(=O)NR^{16}R^{17}$; $-O-C(=O)NR^{16}R^{17}$; $-NR^{16}C(=O)R^{17}$; $-NR^{16}C(=O)R^{17}$; $-NR^{16}S(=O)_2R^{17}$; or $-S(=O)_2NR^{16}R^{17}$; where $-R^{16}$ and $-R^{17}$ have the same meanings as defined above:

- and further where -

---R¹⁵ is a member independently selected from the group consisting of –H; -NR¹⁶R¹⁷; -C(=O)R¹⁶; -OR¹⁶; -(C₁-C₄) alkyl-OR¹⁶; -C(=O)OR¹⁶; -(C₁-C₂) alkyl-C(=O)OR¹⁶; -C(=O)NR¹⁶R¹⁷; -(C₁-C₄) alkyl; -(C₂-C₄) alkenyl; -(CH₂)_u-(C₃-C₇) cycloalkyl where u is 0, 1 or 2; phenyl; benzyl; pyridyl; and quinolinyl; wherein said alkyl, alkenyl, alkoxy, cycloalkyl, phenyl, benzyl, pyridyl or quinolinyl is substituted with 0 to 3 substituents R¹²; where R¹⁶ and R¹⁷ have the same meanings as defined above; and

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- where -

----R¹² is a member independently selected from the group consisting of -F; -CI;

10 -CO₂R¹⁸; -OR¹⁶; -CN; -C(=O)NR¹⁸R¹⁹; -NR¹⁸R¹⁹; -NR¹⁸C(=O)R¹⁹; -NR¹⁸C(=O)OR¹⁹;

-NR¹⁸S(=O)_pR¹⁹; -S(=O)_pNR¹⁸R¹⁹, where p is 1 or 2; -(C₁-C₄) alkyl; and -(C₁-C₄) alkoxy in the case where R¹² has the meaning of -OR¹⁶ above and R¹⁶ is defined as -(C₁-C₄) alkyl; wherein said alkyl and alkoxy are each independently substituted with 0 to 3 substituents independently selected from -F; -CI; -(C₁-C₂) alkoxycarbonyl; -(C₁-C₂) alkylcarbonyl; and -(C₁-C₂) alkylcarbonyloxy; where R¹⁶ has the same meaning as defined above; and

- where -

----- R^{18} and R^{19} are independently selected from the group consisting of -H; $-(C_1-C_4)$ alkyl; and phenyl; where said alkyl or phenyl is substituted by 0-3 of -F; or -Cl;

— or in the case where Q1 is phenyl —

20 -(d) R⁵ and R⁶ are taken together to form a moiety which is a member selected from the group consisting of partial Formulas (1.3.1) through (1.3.15):

$$R^{23}$$
 R^{23} R^{23} R^{24} R^{25} R

- --R²⁰ and R²¹ are each a member independently selected from the group consisting of -H; -F; -Cl; -CH₃; -CH₂F; -CHF₂; -CF₃; -OCH₃; and -OCF₃;
- --R²³ and R²⁴ are each independently -H; -CH₃; -OCH₃; -CH₂CH₃; -OCH₂CH₃; -CH₂CH₃; -CH₂CH₃; -CH₂CH₃; -CH₂CH₃; -CH₂CH₃; -CH₂CH₃; -CH₂CH₃; -C(CH₃)₃; or absent, in which case the dashed line - represents a double bond;
- is a moiety comprising a saturated or unsaturated carbon ring system that is a 3- to 7-membered monocyclic, or that is a 7- to 12-membered, fused polycyclic; provided that Q' is not a discontinuous or restricted biaryl moiety as defined under Q' below; and wherein optionally one carbon atom of said carbon ring system may be replaced by a heteroatom selected from N, O, and S; where optionally a second carbon atom thereof, and further optionally a third carbon atom thereof may be replaced by N;

— wherein —

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said moiety defining Q^1 is substituted on any ring or rings thereof by R^4 , R^5 and R^6 , which have the same meaning as defined above;

- is a discontinuous or restricted biaryl moiety consisting of a saturated or unsaturated carbon ring system that is a 3- to 7-membered monocyclic, or that is a 7- to 12-membered, fused polycyclic; wherein optionally one carbon atom of said carbon ring system may be replaced by a heteroatom selected from N, O, and S; where optionally a second carbon atom thereof, and further optionally a third carbon atom thereof may be replaced by N;
- -Z is a member independently selected from the group consisting of

25 — the following —

-(a) the group consisting of partial Formulas (1.1.1) through (1.1.15):

where R^{16} and R^{17} have the same meanings as defined above; and R^{9} has the same meaning as defined below;

--"*" indicates the point of attachment of each partial Formula (1.1.1) through (1.1.15) to the remaining portion of Formula (1.0.0);

is 1, 2, or 3, provided that where q is 2 or 3, R⁹ has the meaning of –H in at least one instance, or two instances, respectively;

--v 0 or 1;

--W³ is -O-; $-N(R^9)-$, where R^9 has the same meaning as defined below; or -OC(=O)-;

--R⁷_A is a member independently selected from the group consisting of

-- the following: --

- $-(C_1-C_6)$ alkyl; $-(C_2-C_6)$ alkenyl; or $-(C_2-C_6)$ alkynyl; where said alkyl, alkenyl or alkynyl is substituted by 0 to 3 substituents R^{10} , where R^{10} has the same meaning as defined above:
- --(3) -(CH₂)_u-(C₃-C₇) cycloalkyl where u is 0, 1 or 2; and further where said (C₃-C₇) cycloalkyl is substituted by 0 to 3 substituents R¹⁰ where R¹⁰ has the same meaning as defined above;

— and —

- --(4) phenyl or benzyl, where said phenyl or benzyl is independently substituted by 0 to 3 substituents R¹⁰ where R¹⁰ has the same meaning as defined above;
- 10 --R⁷_B is a member independently selected from the group consisting of

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- the following: -

--(1) tetrazol-5-yl; 1,2,4-triazol-3-yl; 1,2,4-triazol-3-on-5-yl; 1,2,3-triazol-5-yl; imidazol-2-yl; imidazol-4-yl; imidazolidin-2-on-4-yl; 1,3,4-oxadiazolyl; 1,3,4-oxadiazol-2-on-5-yl; 1,2,4-oxadiazol-3-yl; 1,2,4-oxadiazol-5-on-3-yl; 1,2,4-oxadiazol-5-yl; 1,2,4-oxadiazol-3-on-5-yl; 1,2,5-thiadiazolyl; 1,3,4-thiadiazolyl; morpholinyl; parathiazinyl; oxazolyl; thiazolyl; isothiazolyl; pyrrolyl; pyrazolyl; succinimidyl; glutarimidyl; pyrrolidonyl; 2-piperidonyl; 2-pyridonyl; 4-pyridonyl; pyridazin-3-onyl; pyridyl; pyrimidinyl; pyrazinyl; pyridazinyl;

— and —

--(2) indolyl; indolinyl; isoindolinyl; benzo[b]furanyl; 2,3-dihydrobenzofuranyl; 1,3-dihydroisobenzofuranyl; 2H-1-benzopyranyl; 2-H-chromenyl; chromanyl; benzothienyl; 1H-indazolyl; benzimidazolyl; benzoxazolyl; benzisoxazolyl; benzothiazolyl; benzotriazolyl; benzotriazinyl; phthalazinyl; 1,8-naphthyridinyl; quinolinyl; isoquinolinyl; quinazolinyl; quinoxalinyl; pyrazolo[3,4-d]pyrimidinyl; pyrimido[4,5-d]pyrimidinyl; imidazo[1,2-a]pyridinyl; pyridopyridinyl; and 1H-purinyl;

-- where --

any moiety recited in (1) or (2) above is optionally substituted with respect to (i) any one or more carbon atoms thereof optionally by a substituent R¹⁴ where R¹⁴ has the same meaning as defined above; (ii) any one or more nitrogen atoms thereof that is not a point of attachment of said moiety, optionally by a substituent R¹⁵ where R¹⁵ has the same meaning as defined above, and all tautomer forms thereof; and (iii) any sulfur atom thereof that is not a point of attachment of said moiety, by 0, 1, or 2 oxygen atoms;

- --R⁹ is a member selected from the group consisting of -H; $-(C_1-C_4)$ alkyl; $-(C_3-C_7)$ cycloalkyl; phenyl; benzyl; pyridyl; $-C(=O)OR^{16}$; $-C(=O)R^{16}$; $-OR^{16}$; $-OR^{16}$; $-OR^{16}$; and $-(C_1-C_2)$ alkyl- $-OR^{16}$; where R¹⁶ has the same meaning as defined above;
- $--R^{7}_{C}$ is a member independently selected from the group consisting of the meanings of R^{7}_{A} and the meanings of R^{7}_{B} defined above;

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- and further wherein -



(1.1.15)

--comprises a saturated or unsaturated, 4– to 8–membered monocyclic, or 5– to 10– membered fused or open bicyclic, carbocyclic ring system containing a nitrogen heteroatom as shown in partial Formula (1.1.15); wherein optionally from 1 to 3 carbon atoms of said carbocyclic ring system may be individually replaced by a nitrogen heteroatom; or optionally 1 carbon atom thereof may be replaced by an oxygen heteroatom or by a sulfur heteroatom; or optionally 2 carbon atoms thereof may be individually replaced by a nitrogen heteroatom and an oxygen heteroatom, or by a nitrogen heteroatom and a sulfur heteroatom;

- where -

any moiety of partial Formula (1.1.15) recited above is optionally substituted with respect to (1) any one or more carbon atoms thereof, by a substituent R¹⁴ where R¹⁴ has the same meaning as defined above; (2) any one or more nitrogen atoms thereof by a substituent R¹⁵ where R¹⁵ has the same meaning as defined above, and all tautomer forms, and optionally N-oxide forms thereof; or (3) any sulfur atom thereof by 0, 1, or 2 oxygen atoms;

— and $\mathbb Z$ is further selected from —

-(b) a moiety comprising a member selected from the group consisting of $-O-P(=O)(OH)_2$ (phosphoric); -PH(=O)OH (phosphinic); $-P(=O)(OH)_2$ (phosphoric); $-[P(=O)(OH)-O(C_1-C_4)$ alkyl] (alkylphosphono); $-P(=O)(OH)-O(C_1-C_4)$ alkyl) (alkylphosphinyl); $-P(=O)(OH)NH_2$ (phosphoramido); $-P(=O)(OH)NH(C_1-C_4)$ alkyl and $-P(=O)(OH)NHR^{25}$ (substituted phosphoramido); $-O-S(=O)_2OH$ (sulfuric); $-S(=O)_2OH$ (sulfonic); $-S(=O)_2NHR^{26}$ or $-NHS(=O)_2R^{26}$ (sulfonamido) where R^{26} is $-CH_3$, $-CF_3$, or otoluyl; and acylsulfonamido selected from the group consisting of $-C(=O)NHS(=O)_2R^{25}$; $-C(=O)NHS(=O)_2NH_2$; $-C(=O)NHS(=O)_2NH(C_1-C_4)$ alkyl; $-C(=O)NHS(=O)_2NH(C_1-C_4)$ alkyl; $-S(=O)_2NHC(=O)NH_2$; $-S(=O)_2NHC(=O)NH_2$;

 $-S(=O)_2NHC(=O)NH(C_1-C_4) \ alkyl; \ -S(=O)_2NHC(=O)N[(C_1-C_4) \ alkyl]_2; \ -S(=O)_2NHC(=O)R^{25};$

 $-S(=O)_2NHCN;$ $-S(=O)_2NHC(=S)NH_2;$ $-S(=O)_2NHC(=S)NH(C_1-C_4)$ alkyl;

 $-S(=O)_2NHC(=S)N[(C_1-C_4) \text{ alkyl}]_2$; and $-S(=O)_2NHS(=O)_2R^{25}$;

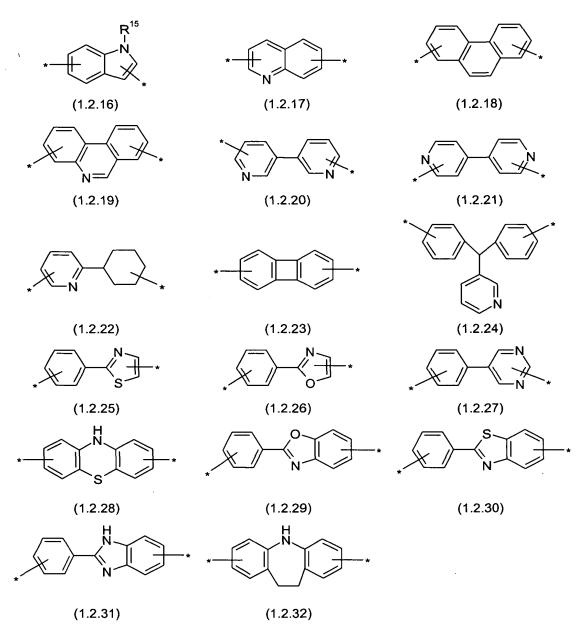
- where -

5 --R²⁵ is -H; -(C₁-C₄) alkyl; phenyl; or -OR¹⁸, where R¹⁸ has the same meaning as defined above;

— or —

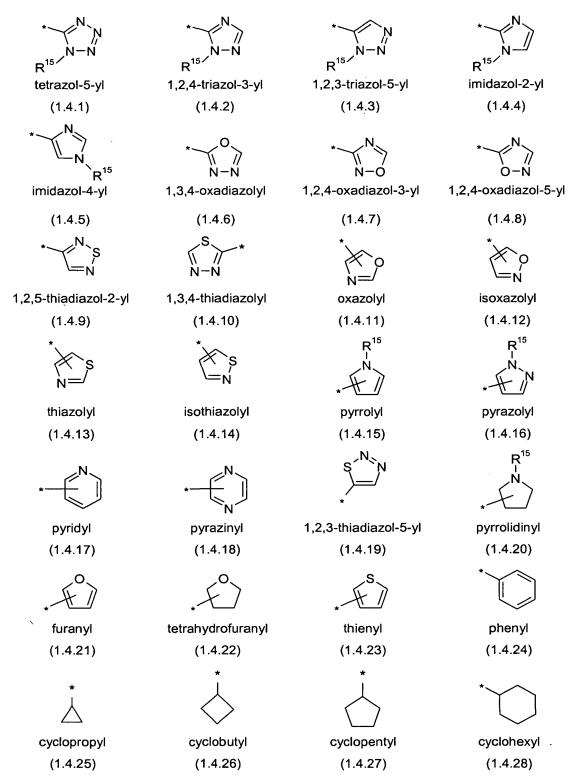
a pharmaceutically acceptable salt thereof.

10 2. A compound according to Claim 1 wherein the group Q^2 comprises a member selected from the group consisting of the following moieties represented by partial Formulas (1.2.1) through (1.2.32):



wherein " \star " is a symbol indicating the two points of attachment of said group \mathbb{Q}^2 to the remaining components of Formula (1.0.0).

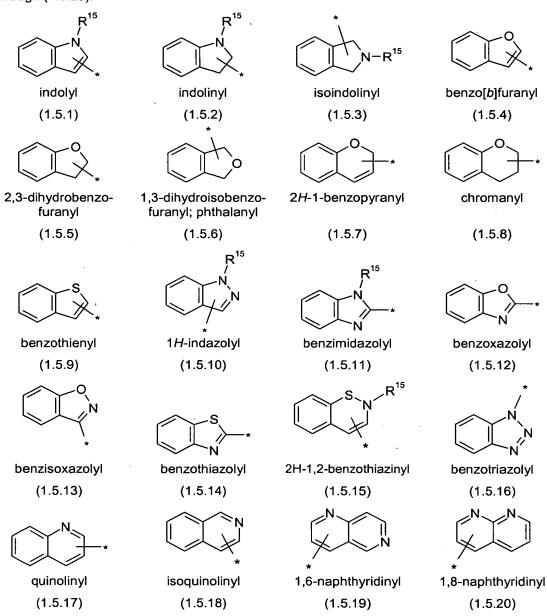
3. A compound according to Claim 1 wherein Z comprises partial Formulas (1.1.4) and (1.1.10) through (1.1.14), and the meaning of R^7_B of partial Formula (1.1.4) where v is 0 or 1, or the meaning of R^7_C of partial Formulas (1.1.10) through (1.1.14) is defined as a member selected from the group consisting of partial Formulas (1.4.1) through (1.4.28):

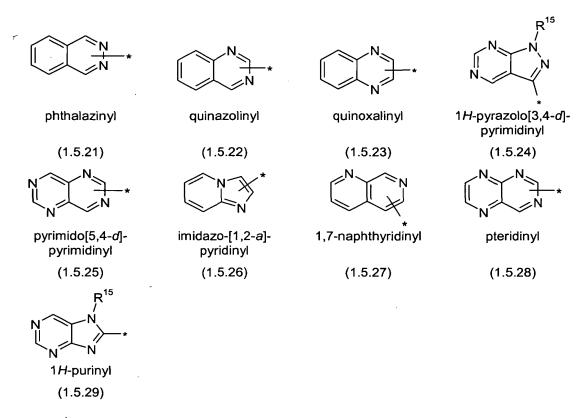


where "*" indicates the point of attachment to the remaining portion of Formula (1.0.0); and where each carbon atom is optionally substituted by a substituent R¹⁴; and where R¹⁴ and R¹⁵

have the same meaning as defined in Claim 1; and all tautomer forms, and optionally N-oxide forms, thereof.

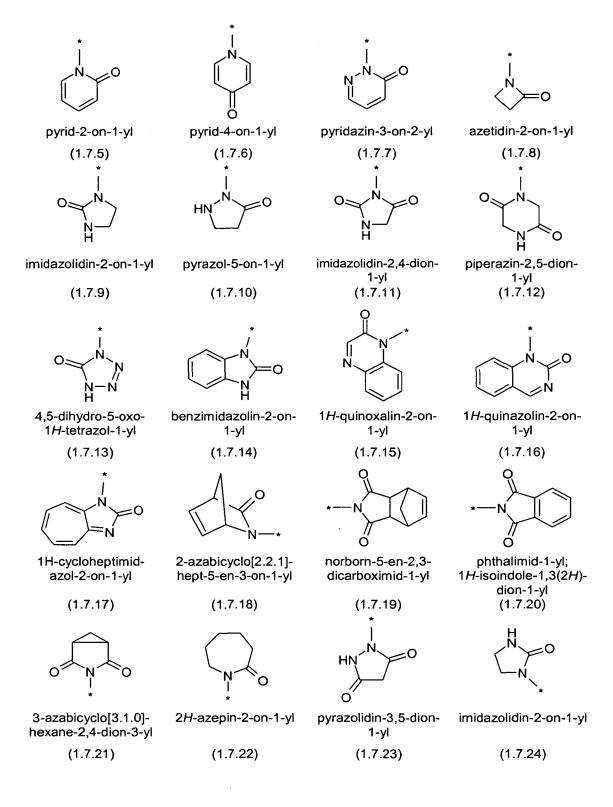
4. A compound according to Claim 1 wherein \mathbb{Z} comprises partial Formulas (1.1.4) and (1.1.10) through (1.1.14) and the meanings of R^7_B and R^7_C in said partial Formulas are each independently a member selected from the group consisting of partial Formulas (1.5.1) through (1.5.29):

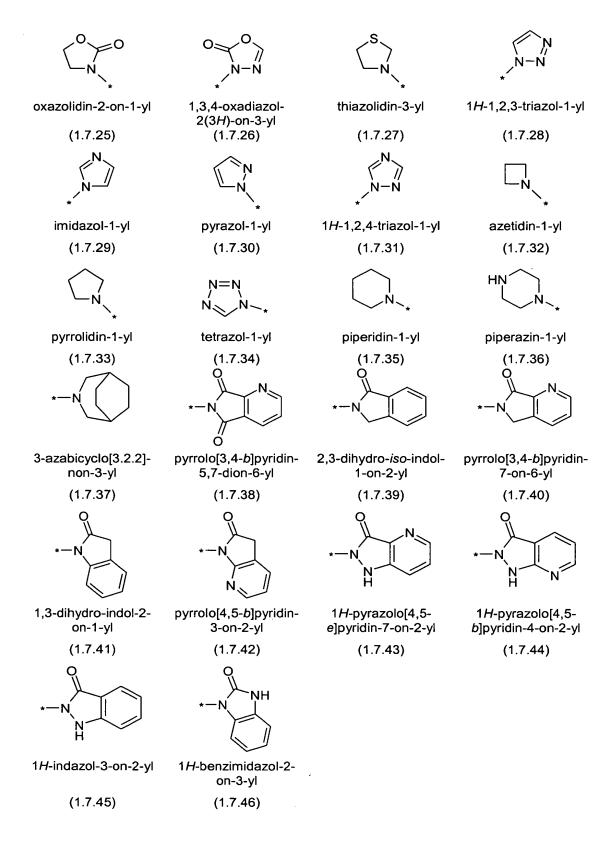




where "*" indicates the point of attachment to the remaining portion of Formula (1.0.0); and where each carbon atom is optionally substituted by a substituent R¹⁴; and where R¹⁴ and R¹⁵ have the same meaning as defined in Claim 1; and all tautomer forms, and optionally N-oxide forms, thereof.

5. A compound according to Claim 1 wherein Z comprises a member selected from the group consisting of partial Formulas (1.7.1) through (1.7.46):





where "*" indicates the point of attachment to the remaining portion of Formula (1.0.0); where each carbon atom is optionally substituted by a substituent R¹⁴; and where each nitrogen atom is optionally substituted by a substituent R¹⁵; where R¹⁴ and R¹⁵ have the same meaning as defined in Claim 1; and all tautomer forms, and optionally N-oxide forms, thereof.

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- 6. A compound according to Claim 1 wherein \mathbb{Q}^1 is phenyl or pyridyl; $\diamond \diamond \mathbb{Q}^2$ is biphenyl, 3-phenyl-pyridine, cyclohexyl-benzene, [2,2']bipyridinyl, bicyclohexyl, naphthalene, or biphenylene; $\diamond \diamond$ j is 1; $\diamond \diamond$ m is 0 or 1; $\diamond \diamond$ n is 1; $\diamond \diamond$ Z is a moiety selected from partial Formulas (1.1.1) through (1.1.3), (1.1.5), (1.1.6), and (1.1.10) through (1.1.14) where R^7_A is (a) -H, or -CH₃ substituted by 0-3 R¹⁰ where R¹⁰ is -F; or is -CH₃ substituted by 0 or 1 R¹⁰ where R^{10} is -CN, $-OR^{16}$ where R^{16} is $-CH_3$ or $-CH_2CH_3$, or $-NR^{16}R^{17}$ or $-NR^{16}C(=O)R^{17}$ where R¹⁶ and R¹⁷ are -H or -CH₃; (b) cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl; or (c) phenyl or benzyl substituted by 0-2 R¹⁰ where R¹⁰ is -F, -Cl, -CF₃, -CH₃, -CH₂OH, -SCH₃, -CN, -NO₂, -OR¹⁶, or -NR¹⁶R¹⁷ where R¹⁶ and R¹⁷ are -H, -CH₃, or -CH₂CH₃; $\diamond \diamond$ R⁹ is -H or $-CH_3$; $\diamond \diamond W^1$ is -O-; $\diamond \diamond g$ is 1 and W^2 is -O- or $-CR^{29}R^{30}$ - where R^{29} and R^{30} are both -H, or g is 0 and W² is thus absent; $\diamond \diamond$ Y is =C(R¹_a)—; $\diamond \diamond$ R¹_a is -H, or -F; $\diamond \diamond$ R^A and R^B are independently -H or -CH₃; or R^A and R^B are taken together to form a -(C₃-C₇) cycloalkyl-spiro moiety; $\diamond \diamond$ one of R^C and R^D is -H and the other is -H or -CH₃; $\diamond \diamond R^1$ and R^2 are -H, -F, or -OCH₃; $\diamond \diamond R^3$ is -H or -CH₃; and $\diamond \diamond R^4$, R^5 and R^6 are -H provided that R^5 and R^6 are not both -H at the same time, -F, -Cl, -OCH₃, -CN; -NO₂, or -C(=O)R³ or -C(=O)OR³ where R³ is -CH₃, or R⁵ and R⁶ are taken together to form a moiety of partial Formula (1.3.1), (1.3.2), (1.3.3), (1.3.4), (1.3.11), (1.3.12), or (1.3.15).
- 7. A compound according to Claim 6 wherein wherein \mathbb{Z} is a moiety of partial Formulas (1.1.1), (1.1.3), (1.1.6) or (1.1.10); \mathbb{R}^9 is $-\mathbb{H}$; \mathbb{R}^A and \mathbb{R}^B are both $-\mathbb{H}$; \mathbb{R}^C and \mathbb{R}^D are both $-\mathbb{H}$; \mathbb{R}^3 is $-\mathbb{H}$; \mathbb{R}^4 is $-\mathbb{H}$; \mathbb{R}^5 is $-\mathbb{H}$, $-\mathbb{F}$, $-\mathbb{C}$ I, $-\mathbb{C}$ N, $-\mathbb{O}$ CH₃, $-\mathbb{C}$ (=O)CH₃, or $-\mathbb{N}$ O₂; \mathbb{R}^6 is $-\mathbb{H}$, provided that \mathbb{R}^5 and \mathbb{R}^6 are not both $-\mathbb{H}$ at the same time, or $-\mathbb{F}$; or \mathbb{R}^5 and \mathbb{R}^6 are taken together to form a moiety of partial Formula (1.3.1) or partial Formula (1.3.11) where \mathbb{R}^{23} and \mathbb{R}^{24} are both absent.
- 8. A compound according to Claim 1 wherein Q' is phenyl or pyridyl; $\diamond \diamond Q^2$ is biphenyl, 3-phenyl-pyridine, cyclohexyl-benzene, [2,2']bipyridinyl, bicyclohexyl, naphthalene, or biphenylene; j is 1; $\diamond \diamond$ m is 0 or 1; $\diamond \diamond$ n is 1; $\diamond \diamond$ z is a moiety selected from partial Formulas (1.1.4) and (1.1.7) where R^7_B is tetrazol-5-yl, 1,2,4-triazol-3-yl, 1,2,4-triazol-3-on-5-yl, imidazol-2-yl, imidazol-4-yl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, oxazolyl, isoxazolyl, pyrrolyl, pyrazolyl, succinimidyl, pyrrolidonyl, thiazolyl, isothiazolyl, 1,2,3-

thiadiazolyl, 1,3,4-thiadiazolyl, pyridyl, pyrazinyl, furanyl, tetrahydrofuranyl, thienyl, indolyl, 2,3-dihydrobenzofuranyl, benzothienyl, 1H-indazolyl, benzimidazolyl, benzoxazolyl, benzotriazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, 1,6-naphthyridinyl, or 1,8naphthyridinyl, all of which are independently substituted by 0 or 1 R¹⁴ where R¹⁴ is -CH₃, -OR¹⁶ where R¹⁶ is -H or -CH₃, oxo (=O), -C(=O)OR¹⁶ where R¹⁶ is -H or -CH₃, $\diamond \diamond$ R⁹ is -H or -CH₃; $\diamond \diamond$ W¹ is -O-; $\diamond \diamond$ g is 1 and W² is -O- or -CR²⁹R³⁰- where R²⁹ and R³⁰ are both –H, or g is 0 and W² is thus absent; $\diamond \diamond$ Y is =C(R¹_a)—; $\diamond \diamond$ R¹_a is –H; or –F; $\diamond \diamond$ R^A and RB are independently -H or -CH3; or RA and RB are taken together to form a -(C_3 - C_7) cycloalkyl-spiro moiety; $\diamond \diamond$ one of R^C and R^D is -H and the other is -H or $-CH_3$; $\diamond \diamond$ R^1 and R^2 are -H, -F, or $-OCH_3$; $\diamond \diamond R^3$ is -H or $-CH_3$; and $\diamond \diamond R^4$, R^5 and R^6 are -H provided that R⁵ and R⁶ are not both -H at the same time, -F, -Cl, -OCH₃, -CN; -NO₂, or -C(=O)R³ or -C(=O)OR3 where R3 is -CH3; or R5 and R6 are taken together to form a moiety of partial Formula (1.3.1), (1.3.2), (1.3.3), (1.3.4), (1.3.11), (1.3.12), or (1.3.15).

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- 9. A compound according to Claim 8 wherein R⁹ is –H; R^A and R^B are both –H; R^C and R^D are both -H; R³ is –H; R⁴ is –H; R⁵ is –H, –F, –Cl, –CN, –OCH₃, –C(=O)CH₃, or –NO₂; R⁶ is –H, provided that R⁵ and R⁶ are not both –H at the same time, or –F; or R⁵ and R⁶ are taken together to form a moiety of partial Formula (1.3.1) or partial Formula (1.3.11) where R²³ and R²⁴ are both absent.
- 10. A compound according to Claim 1 wherein \mathbb{Q}^1 is phenyl or pyridyl; $\diamond \diamond \mathbb{Q}^2$ is biphenyl, 3-phenyl-pyridine, cyclohexyl-benzene, [2,2]bipyridinyl, bicyclohexyl, naphthalene, or biphenylene; $\diamond \diamond$ j is 1; $\diamond \diamond$ m is 0 or 1; $\diamond \diamond$ n is 1; $\diamond \diamond$ Z is a moiety of partial Formula (1.1.15) comprising phthalimid-1-yl, succinimid-1-yl, pyrrolid-2-on-1-yl, glutarimid-1-yl, piperid-2-on-1-yl, pyrid-2-on-1-yl, imidazolidin-2,4-dion-1-yl, 4,5-dihydro-5-oxo-1*H*-tetrazol-1-yl, benzimidazolin-2-on-1-yl, norborn-5-en-2,3-dicarboximid-1-yl, imidazolidin-2-on-1-yl, thiazolidin-3-yl, 1H-1,2,3-triazol-1-yl, 1H-1,2,4-triazol-1-yl, pyrrolidin-1-yl, tetrazol-1-yl, piperidin-1-yl, piperazin-1-yl, 1H-pyrazolo[4,5-e]pyridin-7-on-2-yl, 1H-indazol-3-on-2-yl, 1Hbenzimidazol-2-on-3-yl, or pyrrolo[3,4-b]pyridin-5,7-dion-6-yl; $\diamond \diamond$ W¹ is -O-; $\diamond \diamond$ g is 1 and W^2 is -O- or $-CR^{29}R^{30}-$ where R^{29} and R^{30} are both -H, or g is 0 and W^2 is thus absent; $\diamond \diamond Y$ is $=C(R_a^1)$ -; $\diamond \diamond R_a^1$ is -H; or -F; $\diamond \diamond R^A$ and R^B are independently -H or $-CH_3$; or R^A and R^B are taken together to form a -(C_3 - C_7) cycloalkyl-spiro moiety; $\diamond \diamond$ one of R^C and R^D is -H and the other is –H or -CH₃; $\diamond \diamond R^1$ and R^2 are –H, –F, or -OCH₃; $\diamond \diamond R^3$ is –H or -CH₃; and $\diamond \diamond$ R⁴, R⁵ and R⁶ are -H provided that R⁵ and R⁶ are not both -H at the same time, -F, -Cl, -OCH₃, -CN; -NO₂, or -C(=O)R³ or -C(=O)OR³ where R³ is -CH₃; or R⁵ and R⁶ are taken

together to form a moiety of partial Formula (1.3.1), (1.3.2), (1.3.3), (1.3.4), (1.3.11), (1.3.12), or (1.3.15), where for partial Formulas (1.3.11) and (1.3.12) R^{23} and R^{24} are both absent.

11. A compound according to Claim 10 wherein R^9 is -H; R^A and R^B are both -H; R^C and R^D are both -H; R^3 is -H; R^4 and R^5 are both -H, and R^6 is -F; or R^5 and R^6 are taken together to form a moiety of partial Formula (1.3.1) or (1.3.11).

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12. A compound according to Claim 1 wherein m is 1; $\diamond \diamond$ n is 1; $\diamond \diamond$ W¹ is -O-; $\diamond \diamond$ W² is absent; $\diamond \diamond$ Y is =C(R¹_a)—; $\diamond \diamond$ R¹_a is -H; -CH₃; -CF₃; or -OCH₃; $\diamond \diamond$ one of R^A and R^B.is -H and the other is -CH₃; phenyl; benzyl; pyrrolyl; pyridinyl; or tetrazolyl; or R^A and R^B are taken together to form a -(C₃-C₇) cycloalkyl-spiro moiety; $\diamond \diamond$ R^C and R^D are both -H; $\diamond \diamond$ and R⁵ and R⁶ are taken together to form a moiety selected from the group consisting of partial Formulas (1.3.1) through (1.3.4), (1.3.11), (1.3.12), (1.3.14), and (1.3.15) :

where R^{20} and R^{21} are each independently -H; -F; -CH₃; or -OCH₃; and R^{23} and R^{24} are each independently -H; -CH₃; -OCH₃; or absent, in which case the dashed line - - - represents a double bond.

- 13. A compound according to Claim 1 wherein said compound is a member selected from the group consisting of the following:
- 4'-[[[2-[4-Fluorophenoxyl]-pyridine-3-carbonyl]-amino]-methyl]-biphenyl-3-carboxylic acid of Formula (8.5.1);
- 4'-[[[2-Benzo[1,3]dioxol-5-yloxy]-pyridine-3-carbonyl]-amino]-methyl]-biphenyl-3-carboxylic acid of Formula (8.5.2);
- 4'-[[[2-Benzo[1,3]dioxol-5-yloxy]-pyridine-3-carbonyl]-amino]-methyl]-3'-fluoro-biphenyl-3-carboxylic acid of Formula (8.5.3);
- 4'-[[[2-[3-Cyano-phenoxy]-pyridine-3-carbonyl]-amino]-methyl]-biphenyl-3'-fluoro-biphenyl-3-carboxylic acid of Formula (8.5.4);

- [4'-({[2-(Benzo[2,1,3]thiadiazol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-biphenyl-4-yloxy]-acetic acid of Formula (8.5.5);
- [4'-({[2-(Benzo[2,1,3]oxadiazol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-biphenyl-4-yloxy]-acetic acid of Formula (8.5.6);
- 5 [4'-({[2-(Benzo[1,3]dioxol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-biphenyl-4-yloxy]-acetic acid of Formula (8.5.7);
 - (\pm) -2-[4'-({[2-(Benzo[1,3]dioxol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-2-fluorobiphenyl-4-yloxy]-propionic acid of Formula (8.5.8);
- (±)-2-(Benzo[1,3]dioxol-5-yloxy)-N-(2'-fluoro-4'[1-(1H-tetrazol-5-yl)-ethoxy]-biphenyl-10 4-ylmethyl}-nicotinamide of Formula (8.5.9);
 - (\pm) -2-[4'-({[2-(Benzo[1,3]dioxol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-3'-fluoro-biphenyl-2-yloxy]-propionic acid of Formula (8.5.10);
 - (\pm) -2-(Benzo[1,3]dioxol-5-yloxy)-N-(2'-fluoro-4'[1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethoxy]-biphenyl-4-ylmethyl}-nicotinamide of Formula (8.5.11);
- 15 (±)-N-[4'-(1-Carbamoyl-ethoxy)-2'-fluoro-biphenyl-4-ylmethyl]-2-(3-cyano-phenoxy)-nicotinamide of Formula (8.5.12);
 - (\pm)-2-[2,3'-Difluoro-4'-({[2-(3-methoxy-phenoxy)-pyridine-3-carbonyl]-amino}-methyl)-biphenyl-4-yloxy]-propionic acid of Formula (8.5.13);
- 2-(Benzo[1,3]dioxol-5-yloxy)-N-(4'-carbamoylmethyl-3-fluoro-biphenyl-4-ylmethyl)-20 nicotinamide of Formula (8.5.14);
 - [4'-({[2-(3-Cyano-phenoxy)-3-carbonyl]-amino}-methyl)-3'-fluoro-biphenyl-4-yl]-acetic acid of Formula (8.5.15);
 - 2-(Benzo[1,3]dioxol-5-yloxy)-N-{4'-[(2-cyano-benzoylamino)-methyl]-2'-fluoro-biphenyl-4-ylmethyl)-5-fluoro-nicotinamide of Formula (8.5.16);
- 25 Pyridine-2-carboxylic acid (3'-fluoro-4'-{[2-(4-fluoro-phenoxy)-nicotinamide]-methyl}-biphenyl-4-ylmethyl)-amide of Formula (8.5.17);
 - 2-(Benzo[1,3]dioxol-5-yloxy)-N-{2'-fluoro-4'-[1-methyl-1-(1H-tetrazol-5-yl)-ethyl]-biphenyl-4-ylmethyl}-nicotinamide of Formula (8.5.18);
- 5-Fluoro-N-(3-fluoro-4'-{[(5-methyl-4H-[1,2,4]triazole-3-carbonyl)-amino]-methyl}-30 biphenyl-4-ylmethyl)-2-(3-methoxy-phenoxy)-nicotinamide of Formula (8.5.19);

- 2-(Benzo[1,3]dioxol-5-yloxy)-N-{2'-fluoro-4'-{(2-methoxy-benzoylamino)-methyl]-biphenyl-4-ylmethyl}-nicotinamide of Formula (8.5.20);
- N-[4'-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2'-fluoro-biphenyl-4-ylmethyl]-2-(4-fluoro-phenoxy)-nicotinamide of Formula (8.5.21);
- 5 N-(2'-Fluoro-4'-{[(3H-imidazole-4-carbonyl)-amino]-methyl}-biphenyl-4-ylmethyl)-2-(3-nitro-phenoxy)-nicotinamide of Formula (8.5.22);
 - (\pm) -3-[4'-({[2-(3-Chloro-4-fluoro-phenoxy)-pyridine-3-carbonyl]-amino}-methyl)-2-fluoro-biphenyl-4-yloxy]-butyric acid of Formula (8.5.23);
- 2-[4'-({[2-Benzo[2,1,3]thiadiazol-5-yloxy)-pyridine3-carbonyl]-amino}-methyl)-2-fluoro-10 biphenyl-4-yl]-2-methyl-propionic acid of Formula (8.5.24);
 - (\pm) -2-[4'-({[2-(Benzo[2,1,3]oxadiazol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-2-fluoro-biphenyl-4-yloxy]-propionic acid of Formula (8.5.25);
 - (\pm) -2-[3'-Fluoro-4'-({[2-(2-methyl-2H-benzotriazol-5-yloxy)-pyridine-3-carbonyl]-amino}-methyl)-biphenyl-4-yloxy]-propionic acid of Formula (8.5.26);
 - 2-(3-Cyano-phenoxy)-N-{2'-fluoro-4'[(pyridin-2-ylmethyl)-carbamoyl]-biphenyl-4-ylmethyl}-nicotinamide of Formula (8.5.27);

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- 2-(Benzo[1,3]dioxol-5-yloxy)-N-{2'-fluoro-4'-[(quinolin-2-ylmethyl)-carbamoyl]-biphenyl-4-ylmethyl}-nicotinamide of Formula (8.5.28);
- 5-Fluoro-2-(4-fluoro-phenoxy)N-[3-fluoro-3'-(1H-tetrazol-5-yl)-biphenyl-4-ylmethyl]-nicotinamide of Formula (8.5.29);
 - N-{3-Fluoro-4'-[(1-hydroxy-pyridin-2-ylmethyl)-carbamoyl]-biphenyl-4-ylmethyl}-2-(3-methoxy-phenoxy)-nicotinamide of Formula (8.5.30);
 - $\label{eq:continuous} $$(\pm)-N-[3-Fluoro-4'-(2-hydroxy-1,2-dimethyl-propoxy)-biphenyl-4-ylmethyl]-2-(4-fluoro-phenoxy)-nicotinamide of Formula (8.5.31);$
- N-[2'-Fluoro-4'-(1-hydroxy-1-methyl-ethyl)-biphenyl-4-ylmethyl]-2-(4-fluoro-phenoxy)-nicotinamide of Formula (8.5.32); and
 - 2-(3-Chloro-4-fluoro-phenoxy)-N-[4'-(pyridin-2-ylmethoxy)-biphenyl-4-ylmethyl]-nicotinamide of Formula (8.5.33).
- 14. A method of treating a subject suffering from a disease, disorder or condition 30 mediated by the PDE4 isozyme, including the D subtype thereof, whereby it regulates the activation and degranulation of eosinophils, comprising administering to said subject in need

of said treatment a therapeutically effective amount of a compound of Formula (1.0.0) as defined in Claim 1.

15. A pharmaceutical composition for use in treating a subject suffering from a disease, disorder or condition mediated by the PDE4 isozyme, including the D subtype thereof, whereby it regulates the activation and degranulation of eosinophils, comprising a therapeutically effective amount of a compound of Formula (1.0.0) as defined in Claim 1, together with a pharmaceutically acceptable carrier therefor.

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- 16. A method according to Claim 14 wherein said disease, disorder, or condition comprises one or more members selected from the group consisting of:
- asthma of whatever type, etiology, or pathogenesis; or asthma that is a member selected from the group consisting of atopic asthma; non-atopic asthma; allergic asthma; atopic, bronchial, IgE-mediated asthma; bronchial asthma; essential asthma; true asthma; intrinsic asthma caused by pathophysiologic disturbances; extrinsic asthma caused by environmental factors; essential asthma of unknown or inapparent cause; non-atopic asthma; bronchitic asthma; emphysematous asthma; exercise-induced asthma; occupational asthma; infective asthma caused by bacterial, fungal, protozoal, or viral infection; non-allergic asthma; incipient asthma; wheezy infant syndrome;
 - chronic or acute bronchoconstriction; chronic bronchitis; small airways obstruction; and emphysema;
 - obstructive or inflammatory airways diseases of whatever type, etiology, or pathogenesis; or an obstructive or inflammatory airways disease that is a member selected from the group consisting of asthma; pneumoconiosis; chronic eosinophilic pneumonia; chronic obstructive pulmonary disease (COPD); COPD that includes chronic bronchitis, pulmonary emphysema or dyspnea associated therewith; COPD that is characterized by irreversible, progressive airways obstruction; adult respiratory distress syndrome (ARDS), and exacerbation of airways hyper-reactivity consequent to other drug therapy;
 - pneumoconiosis of whatever type, etiology, or pathogenesis; or pneumoconiosis that is a member selected from the group consisting of aluminosis or bauxite workers' disease; anthracosis or miners' asthma; asbestosis or steam-fitters' asthma; chalicosis or flint disease; ptilosis caused by inhaling the dust from ostrich feathers; siderosis caused by the inhalation of iron particles; silicosis or grinders' disease; byssinosis or cotton-dust asthma; and talc pneumoconiosis;
 - bronchitis of whatever type, etiology, or pathogenesis; or bronchitis that is a member selected from the group consisting of acute bronchitis; acute laryngotracheal bronchitis; arachidic bronchitis; catarrhal bronchitis; croupus bronchitis; dry bronchitis;

infectious asthmatic bronchitis; productive bronchitis; staphylococcus or streptococcal bronchitis; and vesicular bronchitis;

- bronchiectasis of whatever type, etiology, or pathogenesis; or bronchiectasis that is a member selected from the group consisting of cylindric bronchiectasis; sacculated bronchiectasis; fusiform bronchiectasis; capillary bronchiectasis; cystic bronchiectasis; dry bronchiectasis; and follicular bronchiectasis;
- seasonal allergic rhinitis; or perennial allergic rhinitis; or sinusitis of whatever type, etiology, or pathogenesis; or sinusitis that is a member selected from the group consisting of purulent or nonpurulent sinusitis; acute or chronic sinusitis; and ethmoid, frontal, maxillary, or sphenoid sinusitis;
- rheumatoid arthritis of whatever type, etiology, or pathogenesis; or rheumatoid arthritis that is a member selected from the group consisting of acute arthritis; acute gouty arthritis; chronic inflammatory arthritis; degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis;
- gout, and fever and pain associated with inflammation;

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- an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the group consisting of eosinophilia; pulmonary infiltration eosinophilia; Loffler's syndrome; chronic eosinophilic pneumonia; tropical pulmonary eosinophilia; bronchopneumonic aspergillosis; aspergilloma; granulomas containing eosinophils; allergic granulomatous angiitis or Churg-Strauss syndrome; polyarteritis nodosa (PAN); and systemic necrotizing vasculitis;
 - atopic dermatitis; or allergic dermatitis; or allergic or atopic eczema;
- urticaria of whatever type, etiology, or pathogenesis; or urticaria that is a member selected from the group consisting of immune-mediated urticaria; complement-mediated urticaria; urticariogenic material-induced urticaria; physical agent-induced urticaria; stress-induced urticaria; idiopathic urticaria; acute urticaria; chronic urticaria; angioedema; cholinergic urticaria; cold urticaria in the autosomal dominant form or in the acquired form; contact urticaria; giant urticaria; and papular urticaria;
- conjunctivitis of whatever type, etiology, or pathogenesis; or conjunctivitis that is a member selected from the group consisting of actinic conjunctivitis; acute catarrhal conjunctivitis; acute contagious conjunctivitis; allergic conjunctivitis; atopic conjunctivitis; chronic catarrhal conjunctivitis; purulent conjunctivitis; and vernal conjunctivitis;
- —uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis;

iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis; choroiditis; and chorioretinitis;

- psoriasis;

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- multiple sclerosis of whatever type, etiology, or pathogenesis; or multiple sclerosis that is a member selected from the group consisting of primary progressive multiple sclerosis; and relapsing remitting multiple sclerosis;
- autoimmune/inflammatory diseases of whatever type, etiology, or pathogenesis; or an autoimmune/inflammatory disease that is a member selected from the group consisting of autoimmune hematological disorders; hemolytic anemia; aplastic anemia; pure red cell anemia; idiopathic thrombocytopenic purpura; systemic lupus erythematosus; polychondritis; scleroderma; Wegner's granulomatosis; dermatomyositis; chronic active hepatitis; myasthenia gravis; Stevens-Johnson syndrome; idiopathic sprue; autoimmune inflammatory bowel diseases; ulcerative colitis; Crohn's disease; endocrin opthamopathy; Grave's disease; sarcoidosis; alveolitis; chronic hypersensitivity pneumonitis; primary biliary cirrhosis; juvenile diabetes or diabetes mellitus type I; anterior uveitis; granulomatous or posterior uveitis; keratoconjunctivitis sicca; epidemic keratoconjunctivitis; diffuse interstitial pulmonary fibrosis or interstitial lung fibrosis; idiopathic pulmonary fibrosis; cystic fibrosis; psoriatic arthritis; glomerulonephritis with and without nephrotic syndrome; acute glomerulonephritis; idiopathic nephrotic syndrome; minimal change nephropathy; inflammatory/hyperproliferative skin diseases; psoriasis; atopic dermatitis; contact dermatitis; allergic contact dermatitis; benign familial pemphigus; pemphigus erythematosus; pemphigus foliaceus; and pemphigus vulgaris;
 - prevention of allogeneic graft rejection following organ transplantation;
- inflammatory bowel disease (IBD) of whatever type, etiology, or pathogenesis; or
 inflammatory bowel disease that is a member selected from the group consisting of ulcerative colitis (UC); collagenous colitis; colitis polyposa; transmural colitis; and Crohn's disease (CD);.
 - septic shock of whatever type, etiology, or pathogenesis; or septic shock that is a member selected from the group consisting of renal failure; acute renal failure; cachexia; malarial cachexia; hypophysial cachexia; uremic cachexia; cardiac cachexia; cachexia suprarenalis or Addison's disease; cancerous cachexia; and cachexia as a consequence of infection by the human immunodeficiency virus (HIV);
 - -- liver injury;
 - pulmonary hypertension; and hypoxia-induced pulmonary hypertension;

- bone loss diseases; primary osteoporosis; and secondary osteoporosis;
- central nervous system disorders of whatever type, etiology, or pathogenesis; or a central nervous system disorder that is a member selected from the group consisting of depression; Parkinson's disease; learning and memory impairment; tardive dyskinesia; drug dependence; arteriosclerotic dementia; and dementias that accompany Huntington's chorea, Wilson's disease, paralysis agitans, and thalamic atrophies;

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- infection, especially infection by viruses wherein such viruses increase the production of TNF- α in their host, or wherein such viruses are sensitive to upregulation of TNF- α in their host so that their replication or other vital activities are adversely impacted, including a virus which is a member selected from the group consisting of HIV-1, HIV-2, and HIV-3; cytomegalovirus, CMV; influenza; adenoviruses; and Herpes viruses, including Herpes zoster and Herpes simplex;
- yeast and fungus infections wherein said yeast and fungi are sensitive to upregulation by TNF- α or elicit TNF- α production in their host, when administered in conjunction with other drugs of choice for the treatment of systemic yeast and fungus infections, including but not limited to, polymixins, Polymycin B; imidazoles, clotrimazole, econazole, miconazole, and ketoconazole; triazoles, fluconazole and itranazole; and amphotericins, Amphotericin B and liposomal Amphotericin B; and
- ischemia-reperfusion injury; autoimmune diabetes; retinal autoimmunity; chronic
 lymphocytic leukemia; HIV infections; lupus erythematosus; kidney and ureter disease; urogenital and gastrointestinal disorders; and prostate diseases.
 - 17.. A method of treatment according to Claim 16 wherein said disease, disorder, or condition is a member selected from the group consisiting of (1) inflammatory diseases and conditions comprising: joint inflammation, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and conditions comprising: asthma, acute respiratory distress syndrome, chronic pulmonary inflammatory disease, bronchitis, chronic obstructive airway disease, and silicosis; (3) infectious diseases and conditions comprising: sepsis, septic shock, endotoxic shock, gram negative sepsis, toxic shock syndrome, fever and myalgias due to bacterial, viral or fungal infection, and influenza; (4) immune diseases and conditions comprising: autoimmune diabetes, systemic lupus erythematosis, graft vs. host reaction, allograft rejections, multiple sclerosis, psoriasis, and allergic rhinitis; and (5) other diseases and conditions comprising: bone resorption diseases; reperfusion injury; cachexia secondary to infection or malignancy; cachexia secondary to human acquired immune deficiency syndrome (AIDS), human immunodeficiency virus (HIV)

infection, or AIDS related complex (ARC); keloid formation; scar tissue formation; type 1 diabetes mellitus; and leukemia.

- 18. The combination of a compound of Formula (1.0.0) as defined in Claim 1 together with one or more members selected from the group consisting of the following:
- (a) Leukotriene biosynthesis inhibitors: 5-lipoxygenase (5-LO) inhibitors and 5-lipoxygenase activating protein (FLAP) antagonists selected from the group consisting of zileuton; ABT-761; fenleuton; tepoxalin; Abbott-79175; Abbott-85761; *N*-(5-substituted)-thiophene-2-alkylsulfonamides of Formula (5.2.8); 2,6-di-*tert*-butylphenol hydrazones of Formula (5.2.10); the class of methoxytetrahydropyrans which includes Zeneca ZD-2138 of Formula (5.2.11); the compound SB-210661 of Formula (5.2.12) and the class to which it belongs; the class of pyridinyl-substituted 2-cyanonaphthalene compounds to which L-739,010 belongs; the class of 2-cyanoquinoline compounds to which L-746,530 belongs; the classes of indole and quinoline compounds to which MK-591, MK-886, and BAY x 1005 belong;
- (b) Receptor antagonists for leukotrienes LTB₄, LTC₄, LTD₄, and LTE₄ selected from the group consisting of the phenothiazin-3-one class of compounds to which L-651,392 belongs; the class of amidino compounds to which CGS-25019c belongs; the class of benzoxaolamines to which ontazolast belongs; the class of benzenecarboximidamides to which BIIL 284/260 belongs; and the classes of compounds to which zafirlukast, ablukast, montelukast, pranlukast, verlukast (MK-679), RG-12525, Ro-245913, iralukast (CGP 45715A), and BAY x 7195 belong;
 - (c) PDE4 inhibitors including inhibitors of the isoform PDE4D;
 - (d) 5-Lipoxygenase (5-LO) inhibitors; or 5-lipoxygenase activating protein (FLAP) antagonists;
- 25 (e) Dual inhibitors of 5-lipoxygenase (5-LO) and antagonists of platelet activating factor (PAF);
 - (f) Leukotriene antagonists (LTRAs) including antagonists of LTB₄, LTC₄, LTD₄, and LTE₄;
 - (g) Antihistaminic H₁ receptor antagonists including cetirizine, loratadine, desloratadine, fexofenadine, astemizole, azelastine, and chlorpheniramine;
- 30 (h) Gastroprotective H₂ receptor antagonists;
 - (i) α_1 and α_2 —adrenoceptor agonist vasoconstrictor sympathomimetic agents administered orally or topically for decongestant use, including propylhexedrine, phenylephrine, phenylpropanolamine, pseudoephedrine, naphazoline hydrochloride,

- oxymetazoline hydrochloride, tetrahydrozoline hydrochloride, xylometazoline hydrochloride, and ethylnorepinephrine hydrochloride;
- (j) α_1 and α_2 —adrenoceptor agonists in combination with inhibitors of 5-lipoxygenase (5-LO);
- 5 (k) Anticholinergic agents including ipratropium bromide;
 - (I) β_1 to β_4 —adrenoceptor agonists including isoprenaline, albuterol, salbutamol, formoterol, salmeterol, terbutaline, orciprenaline, bitolterol mesylate, and pirbuterol;
 - (m) Theophylline and aminophylline;
 - (n) Sodium cromoglycate;
- 10 (o) Muscarinic receptor (M1, M2, and M3) antagonists;
 - (p) COX-1 inhibitors (NSAIDs); COX-2 selective inhibitors including refecoxib; and nitric oxide NSAIDs;
 - (q) Insulin-like growth factor type I (IGF-1) mimetics;
 - (r) Ciclesonide;
- 15 (s) Inhaled glucocorticoids with reduced systemic side effects, including flunisolide, triamcinolone acetonide, beclomethasone dipropionate, budesonide, fluticasone propionate, and mometasone furoate;
 - (t) Tryptase inhibitors;
 - (u) Platelet activating factor (PAF) antagonists;
- 20 (v) Monoclonal antibodies against endogenous inflammatory entities;
 - (w) IPL 576;
 - (x) Anti-tumor necrosis factor (TNFα) agents including Etanercept, Infliximab, and D2E7;
 - (y) DMARDs including Leflunomide;
 - (z) TCR peptides;
- 25 (aa) Interleukin converting enzyme (ICE) inhibitors;
 - (bb) IMPDH inhibitors;
 - (cc) Adhesion molecule inhibitors including VLA-4 antagonists;
 - (dd) Cathepsins;
 - (ee) MAP kinase inhibitors;

- (ff) Glucose-6 phosphate dehydrogenase inhibitors;
- (gg) Kinin-B₁ and B₂ -receptor antagonists;
- (hh) Gold in the form of an aurothio group together with various hydrophilic groups;
- (ii) Immunosuppressive agents, e.g., cyclosporine, azathioprine, and methotrexate;
- 5 (jj) Anti-gout agents, e.g., colchicine;
 - (kk) Xanthine oxidase inhibitors, e.g., allopurinol;
 - (II) Uricosuric agents, e.g., probenecid, sulfinpyrazone, and benzbromarone;
 - (mm) Antineoplastic agents, especially antimitotic drugs including the vinca alkaloids such as vinblastine and vincristine;
- 10 (nn) Growth hormone secretagogues;
 - (oo) Inhibitors of matrix metalloproteases (MMPs), *i.e.*, the stromelysins, the collagenases, and the gelatinases, as well as aggrecanase; especially collagenase-1 (MMP-1), collagenase-2 (MMP-8), collagenase-3 (MMP-13), stromelysin-1 (MMP-3), stromelysin-2 (MMP-10), and stromelysin-3 (MMP-11);
- 15 (pp) Transforming growth factor (TGFβ);
 - (qq) Platelet-derived growth factor (PDGF);
 - (rr) Fibroblast growth factor, e.g., basic fibroblast growth factor (bFGF);
 - (ss) Granulocyte macrophage colony stimulating factor (GM-CSF);
 - (tt) Capsaicin cream;
- 20 (uu) Anti-emetic agents including NK-1 receptor antagonists and D-4418; and
 - (vv) Anti-depressants.